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08/876,276 06/16/97 SHORT

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EXAMINER

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| ART UNIT | PAPER NUMBER |
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1652

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DATE MAILED:

10/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

| | | |
|------------------------------|--------------------------------------|-------------------------------------|
| Office Action Summary | Application No. 08/876,276 | Applicant(s) Short et al. |
| | Examiner Peter Tung | Group Art Unit 1652 |

Responsive to communication(s) filed on _____.

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 19-45 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 19-45 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 12

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1652

DETAILED ACTION

1. Claims 19-45 are pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 19 recites the limitation "the activity of interest" in lines 3-4 of the instant claim.

There is insufficient antecedent basis for this limitation in the claim.

4. Claim 21 recites the limitation "the enzyme" in line 1 of the instant claim. There is insufficient antecedent basis for this limitation in the claim.

5. Claims 36 and 38 recite the limitation "the enzyme" in line 1 of the instant claims. There is insufficient antecedent basis for this limitation in the claim.

6. Claim 36 recites the limitation "the mutagenized DNA" in line 1 of the instant claim.

There is insufficient antecedent basis for this limitation in the claim.

7. Claims 38 and 41 recite the limitation "the non-mutagenized DNA" in lines 2 and 3, respectively, of the instant claims. There is insufficient antecedent basis for this limitation in the claim.

Art Unit: 1652

8. Claim 40 is indefinite as what is meant by "at least one mutation." As one mutation may be a one nucleotide change or a deletion of many consecutive nucleotides, the metes and bounds of "at least one mutation" are not clearly defined.

9. Claim 32 and 39 are unclear regarding stable insertion of or stably inserting substrate. It is unclear what Applicants mean when a substrate is "stably inserted."

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening DNA to identify lipases, esterases, glycosidases, proteases, and monooxygenases through the use of bioactive fluorescent substrates does not reasonably provide enablement for the use of said screening method to identify glycosyl transferases, phosphatases, kinases, diarylpropane peroxidases, epoxide hydrolases, nitrile hydratases, nitrilases, transaminases, amidases and acylases. This rejection is explained in the previous Office action.

12. Applicants argue that the instant specification discloses fluorescent substrates that are fluorescent in the presence of glycosyl transferases, phosphatases, kinases, diarylpropane peroxidases, epoxide hydrolases, nitrile hydratases, nitrilases, transaminases, amidases and acylases. Applicants further argue that such fluorescent substrates are well known in the art.

Art Unit: 1652

13. Applicant's arguments filed 6/8/00 have been fully considered but they are not persuasive. No examples of fluorescent substrates are disclosed in the specification for the stated enzymes. To support that such substrates are well known in the art at the time of the invention, Applicants are invited to identify those fluorescent substrates and the enzymes which catalyze them.

14. Claims 32-34 and 39 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. The "stable insertion" of substrate or "stably inserting substrate" is not originally disclosed in the instant specification.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

16. Claims 19, 20, 22, 24-29, 35, 37 and 42-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Thompson et al. (U.S. Patent No. 5,824,485). This rejection is explained in the previous Office action. With regard to claims 42-45, Thompson et al. further teach (col. 4, lines

Art Unit: 1652

55-60) producing expression libraries from one or more species of donor organisms, especially those that cannot be cultured in the laboratory.

17. Applicants argue that the instant reference does anticipate the instant claims as Thompson et al. teach libraries which contain expression constructs prepared from genetic material obtained from one or more species of donor organisms and where in many cases the clones do not each contained DNA from a single organism but are synthetically produced. Such synthetic libraries would encode novel pathways. Additionally the reference is silent regarding preparing a library of naturally occurring genes or gene pathways in which each clone may contain any type of DNA and wherein the DNA in each clone is obtained from an organism from a mixed population of organisms. Additionally, Thompson et al. fails to suggest a method for high throughput screening, fails to suggest that the natural libraries could produce biomolecules in sufficient amounts to turn over a detectable amount of substrate, and fails to suggest methods useful for causing a fluorescent molecule to enter cells sufficient to conduct high throughput screening.

18. Applicant's arguments filed 6/8/00 have been fully considered but they are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the many cases where the clones do not each contain DNA from a single organism but are synthetically produced) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The use of fluorescence activated cell sorting,

Art Unit: 1652

a high throughput method of screening, to identify cells for specific enzymatic activity would require the fluorescent substrates to enter the cells and be catalyzed in sufficient quantity to be detected. Thompson et al. teaches all these elements, as stated in the previous Office action.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. (U.S. Patent No. 5,824,485) in view of Nader et al.(U.S. Patent No. 5,173,187). This rejection is explained in the previous Office action.

Art Unit: 1652

22. Applicants argue that the instant applications method for identifying an activity of interest using high throughput screening of DNA distinguishes over the disclosure of Thompson et al. Applicants further argue that Nader is silent on screening a library.

23. Applicant's arguments filed 6/8/00 have been fully considered but they are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the many cases where the clones do not each contain DNA from a single organism but are synthetically produced) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The use of fluorescence activated cell sorting, a high throughput method of screening, to identify cells for specific enzymatic activity would require the fluorescent substrates to enter the cells and be catalyzed in sufficient quantity to be detected. Thompson et al. teaches all these elements, as stated in the previous Office action.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

While Nader et al. is silent on screening a library, as stated in the previous Office action, Nader et al. teach the identification of esterases in bacteria by their cleavage of a fluorescent substrate and the isolation of the bacteria by fluorescence activated cell sorting. As Thompson et

Art Unit: 1652

al. teach screening of expression libraries by enzymatic activity and by FACS, one would have been motivated to combine the screening of expression libraries, as taught by Thompson et al., with the method of fluorescent substrates and FACS, as taught by Nader et al., for the benefit of identifying a clone of the expression library which expresses an esterase. One of ordinary skill in the art is motivated to combine the two references as FACS is a method taught by Nader et al. to screen for esterase activity while Thompson et al. teach FACS to screen for esterase activity. One of ordinary skill would have used FACS, as taught by both references, to screen for the specific enzymatic activity of esterases, as taught by Nader et al.

24. Claims 19 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. (U.S. Patent No. 5,824,485). This rejection is explained in the previous Office action.

25. Applicants argue that the instant applications method for identifying an activity of interest using high throughput screening of DNA distinguishes over the disclosure of Thompson et al.

26. Applicant's arguments filed 6/8/00 have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the many cases where the clones do not each contain DNA from a single organism but are synthetically produced) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The use of fluorescence activated cell sorting, a

Art Unit: 1652

high throughput method of screening, to identify cells for specific enzymatic activity would require the fluorescent substrates to enter the cells and be catalyzed in sufficient quantity to be detected. Thompson et al. teaches all these elements, as stated in the previous Office action.

27. Claims 19, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. (U.S. Patent No. 5,824,485) in view of Miao et al. This rejection is explained in the previous Office action.

28. Applicants argue that the deficiencies of Thompson et al. for disclosing or suggesting the instant invention have been discussed previously. Applicants argue that the combined teachings of Thompson and Miao are not sufficient to teach or suggest the instant invention.

29. Applicant's arguments filed 6/8/00 have been fully considered but they are not persuasive. As stated previously, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the many cases where the clones do not each contain DNA from a single organism but are synthetically produced) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The use of fluorescence activated cell sorting, a high throughput method of screening, to identify cells for specific enzymatic activity would require the fluorescent substrates to enter the cells and be catalyzed in sufficient quantity to be detected. Thompson et al. teaches all these elements, as

Art Unit: 1652

stated in the previous Office action. As stated in the previous Office action, the instant claims are unpatentable over Thompson et al. in view of Miao.

30. Claims 19 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. (U.S. Patent No. 5,824,485). This rejection is explained in the previous Office action.

31. Applicants argue that the deficiencies of Thompson et al. for disclosing or suggesting the instant invention have been discussed previously.

32. Applicant's arguments filed 6/8/00 have been fully considered but they are not persuasive. As stated previously, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the many cases where the clones do not each contain DNA from a single organism but are synthetically produced) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The use of fluorescence activated cell sorting, a high throughput method of screening, to identify cells for specific enzymatic activity would require the fluorescent substrates to enter the cells and be catalyzed in sufficient quantity to be detected. Thompson et al. teaches all these elements, as stated in the previous Office action.

Art Unit: 1652

33. Claims 19 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. (U.S. Patent No. 5,824,485) in view of Miao et al. This rejection is explained in the previous Office action.

34. Applicants argue that the deficiencies of Thompson et al. for disclosing or suggesting the instant invention have been discussed previously. Applicants further argue that the combined teachings of Thompson et al. and Miao et al. are not sufficient to disclose or suggest the instant invention.

35. Applicant's arguments filed 6/8/00 have been fully considered but they are not persuasive. As stated previously, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the many cases where the clones do not each contain DNA from a single organism but are synthetically produced) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The use of fluorescence activated cell sorting, a high throughput method of screening, to identify cells for specific enzymatic activity would require the fluorescent substrates to enter the cells and be catalyzed in sufficient quantity to be detected. Thompson et al. teaches all these elements, as stated in the previous Office action.

Art Unit: 1652

Allowable Subject Matter

36. Claim 40 is allowable over the prior art of record.
37. No claims are allowed.

Conclusion

38. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

39. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

Art Unit: 1652

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
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